mingham antenatal patients is 34% (Table I) compared with 13% in London (Williams and Leigh, 1966). An identical technique was used in Birmingham and London. The large number of sulphonamide-resistant strains is probably the reason for the relatively poor cure rate obtained with long-acting sulphonamide alone (Table II). Grüneberg and Brumfitt (1967) found a cure rate of 88% with sulfadoxine when treating general-practice patients; almost all of these organisms were sulphonamide-sensitive.

The failures of treatment with sulfametopyrazine occurred in sulphonamide-resistant strains (Table III). Possibly in areas with a high incidence of sulphonamide-sensitive strains the cure rate would be satisfactory with sulphonamide alone, but only 52 (55%) of our 95 patients responded.

Streptomycin produces very high bactericidal levels in the urine (Buggs *et al.*, 1946), and 95% of the organisms isolated were sensitive to streptomycin. Unfortunately, the action is short-lived, and of the 20 patients treated only nine responded. The results with combined therapy were more successful than the other regimens, three-quarters of the infections being eradicated (Table II). This improvement in cure rate was achieved by streptomycin, raising the cure rate of sulphonamide-resistant strains from 18 to 73% (Table III). Alternatively, the sulfametopyrazine raises the cure rate of streptomycin-sensitive strains from 47 to 74%. Development of resistance during treatment is a feature of treatment with both sulphonamide and streptomycin and occurred even when both compounds were used simultaneously.

Toxicity must be considered with particular care in pregnancy because of the risk of damage to the fetus. The possible effects on the neonate from sulphonamide therapy arise from jaundice due to competition between sulphonamide and bilirubin for binding sites (Odell, 1959; Dunn, 1964). None of

our patients, however, was more than 36 weeks pregnant when treated. None of the mothers showed adverse reactions to the sulphonamide.

Neonatal deafness has been recorded following treatment of the mother with streptomycin and its analogues for tuberculosis, but the treatment in these cases has been prolonged and the incidence very low (Adamsons and Joelson, 1966). In the children studied by Conway and Birt (1965) very large doses of streptomycin given to the mother sometimes produced abnormalities in eighth-nerve function tests, but no cases of perceptive deafness were found. It is unlikely that the dose we have used would have a perceptible effect on the fetus.

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Thyroid Scanning with ^{131}Cs

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Summary: Scanning of the thyroid gland after the administration of radioactive caesium (^{131}Cs) was performed in 45 patients; in 38 of these it had been shown that a thyroid nodule failed to accumulate sodium pertechnetate ($^{99\text{m}}\text{Tc}$) or sodium iodide (^{131}I). ^{131}Cs was concentrated in the nodule to a greater degree than in the paranodular thyroid tissue in seven patients, in five of whom thyroid carcinoma was subsequently identified. In five patients ^{131}Cs accumulated in both the nodule and paranodular tissue, while in the other 26 no ^{131}Cs uptake occurred in the nodule. In only one of the latter group was the thyroid lesion malignant. Caesium scanning seems to offer a useful supplementary procedure in the investigation of thyroid nodules.

Introduction

Though organ scanning is proving increasingly popular as a routine investigation for demonstrating space-filling lesions, this procedure does lack specificity when the radionuclides at present commonly available are used. Considerable attention is

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therefore being paid to the development of tumour-seeking isotopes. Several radionuclides have been studied in the past in the hope that specific localization in tumours might be achieved, but few have proved useful. Radioactive ionic caesium (^{131}Cs), used by Charkes *et al.* (1965), was shown to have positive tumour localization in some patients. In similar trials by Uchiyama *et al.* (1969) particular attention was paid to scanning of the thyroid gland. Since these workers claimed a differential uptake of this nuclide between malignant and benign lesions of the thyroid, it seemed important to evaluate further the clinical applications of this technique. Our findings in an initial series of patients suggests that the procedure is indeed of value.

Patients and Methods

Scans of the neck were performed with a Picker Magna-scanner 500 after the intravenous administration of 500 μCi caesium chloride (^{131}Cs). In an initial study of five patients in whom scans were carried out at 30-minute intervals the maximum target/non-target differentiation was observed at two hours after giving the radionuclide.

Radiocaesium scans were performed in 45 patients. In 38 of these this examination was undertaken after the demonstration with $^{99\text{m}}\text{Tc}$ or ^{131}I that one or more palpable nodules

within the thyroid gland comprised non-functioning tissue. These patients with "cold" nodules were classified according to a provisional clinical diagnosis based on their history, the duration of the nodule, and the findings on examination of the thyroid gland. In six patients a confident diagnosis of malignancy was made; this group was designated "clinically malignant." Malignancy appeared likely in another six patients—the "possibly malignant" group—while in seven the diagnosis was less probable—the "malignancy unlikely" group. A confident clinical diagnosis that the nodule was benign was made in another 19 patients, classified as "clinically benign." For all 19 subjects in the first three groups and for five of the clinically benign group a definitive diagnosis was obtained after histological examination of tissue obtained at thyroidectomy or open biopsy of the swelling. ^{131}Cs scans were also performed in six patients in whom there was no thyroid accumulation of ^{131}I or $^{99\text{m}}\text{Tc}$. Of these, four had been given triiodothyronine for a suppression test and two were suffering from subacute thyroiditis. The final patient in the series had a hyperfunctioning thyroid nodule and complete suppression of $^{99\text{m}}\text{Tc}$ uptake in the rest of the gland.

The scans were studied to determine relative ^{131}Cs uptake in the region of the nodule and in the paranodular thyroid tissue; this was facilitated by superimposing the caesium scan on the scan previously obtained with pertechnetate. In this way the nodule was classified as "cold ^{131}Cs " when there was no radiocaesium accumulation in the nodule or as "hot ^{131}Cs " when ^{131}Cs uptake was virtually confined to the nodule. For patients in whom ^{131}Cs accumulated both in the nodule and in the paranodular tissue the scan was classified as "warm ^{131}Cs ."

Results

The results of caesium scanning in patients with a thyroid swelling are summarized in Table I. In the clinically malignant group thyroid carcinoma was identified in the three patients in whom a hot ^{131}Cs scan was obtained. In two of these the lesion was a papillary carcinoma; in the other it was anaplastic. Totally undifferentiated carcinoma was found in the patient in this group in whom no ^{131}Cs accumulation could be demonstrated in the thyroid mass. As this patient also had extensive carcinomatous deposits in the lungs, we were not entirely certain that this was a primary thyroid tumour. In another patient in whom a confident clinical diagnosis of carcinoma had been made and in whom the mass failed to accumulate ^{131}Cs , histological examination after partial thyroidectomy showed autoimmune thyroiditis. The last patient in this group demonstrated avid localized ^{131}Cs uptake in a pattern totally different from the $^{99\text{m}}\text{Tc}$ scan, but this uptake did not align with the palpable nodules. She was classified as "hot" and is discussed in detail below as an illustrative example.

TABLE I.—Results of ^{131}Cs Scans

Initial Clinical Diagnosis	Caesium Scan of Nodule	Final Diagnosis	
		Malignant	Benign
Clinically malignant (6)	Hot ?Hot Cold	3 1 1	— — 1
Possibly malignant (6)	Hot Warm Cold	— — —	1 1 4
Malignancy unlikely (7)	Hot Warm Cold	1 — —	— 1 5
Clinically benign (operated) (5)	Hot Warm Cold	— — —	1 — 4
Clinically benign (not operated) (14)	Hot Warm Cold	— — —	— 3 11

All six patients in the possibly malignant group were found to have a benign adenoma; in four this was associated with a cold Cs scan, in one with a warm ^{131}Cs scan, while the other, because there was significantly greater Cs uptake in the nodule, was considered a hot ^{131}Cs scan.

Five of the seven patients classed under malignancy unlikely had a cold ^{131}Cs scan, and in one it was warm. In these six patients the nodule was benign. In the other patient in this group the scan (Fig. 1) showed an avid uptake of ^{131}Cs in the right upper pole nodule, which had previously been shown not to accumulate $^{99\text{m}}\text{Tc}$. At operation this nodule was found to be papillary carcinoma.

In the clinically benign group 15 cold Cs scans and three warm Cs scans were found. In the remaining patient avid uptake of radiocaesium was noted in the nodule, which, however, proved to be a microfollicular adenoma. In the other four patients in this group who underwent operation the lesion was found to be either an adenoma or intrathyroid haemorrhage.

^{131}Cs scans were performed in the six patients in whom there was no thyroid uptake of $^{99\text{m}}\text{Tc}$ or ^{131}I to determine whether any outline of thyroid morphology could be obtained in these circumstances. In five patients uptake of ^{131}Cs could be seen, though the quality of the scan was poor. In one of these a cold nodule previously demonstrated with $^{99\text{m}}\text{Tc}$ and ^{131}Cs could still be seen after the patient had received liothyronine, 40 μg . eight-hourly for seven days. In two other patients the ^{131}Cs uptake was inadequate to show the thyroid. In the patient with an autonomous hyperfunctioning nodule this nodule could not be identified in the ^{131}Cs scan. In this scan the radioactivity was distributed uniformly throughout the thyroid gland, including the paranodular tissue in which there had been no accumulation of $^{99\text{m}}\text{Tc}$.

We have already referred to one patient in the malignant group in whom difficulty was encountered in evaluating the significance of the ^{131}Cs scan. Details of this patient's history and investigations do, however, illustrate the value of this investigation.

The present study confirms that malignant thyroid tissue is usually associated with a higher ^{131}Cs uptake than normal thyroid tissue or non-malignant lesions of the gland. Hot Cs scans were found in five of the six cases of thyroid carcinoma. Similar hot scans were obtained in 2 of the 32 patients with benign nodules, and in another seven cases some ^{131}Cs accumulation did occur in the nodule. In general, correlation with histological appearances suggested that these benign nodules associated with ^{131}Cs uptake were more cellular and had less colloid than those which failed to accumulate ^{131}Cs . Uchiyama *et al.* found three such "false positives" in their 22 benign nodules.

The role of this technique as a diagnostic procedure is not yet fully ascertained. Certainly, ^{131}Cs uptake is not truly specific to malignant tissue. No study has been made of the mecha-

Fig. 1.—Radiocaesium scan of thyroid demonstrating ^{131}Cs accumulation in a solitary nodule subsequently found to be papillary carcinoma.

nism which results in a higher concentration being achieved in thyroid carcinoma. Charkes *et al.* suggested that it might reflect either the vascularity or the greater alkali metal content of tumours, while Uchiyama *et al.* also pointed out that caesium is an akin element of potassium. The radiocaesium accumulation by the thyroid does not seem to be related to the specific metabolic characteristics of the organ, since this radionuclide was accumulated in glands in which neither ^{99m}Tc nor ^{131}I trapping occurred, though the ^{131}Cs concentration in these glands was less than that in normal thyroid tissue. This observation may possibly prove of some clinical value, as, for example, in the differentiation of localized viral thyroiditis from intrathyroidal haemorrhage, or, of course, when thyroid scanning is desired but not possible because of a suppressed thyroid trapping mechanism.

The main indication for ^{131}Cs scanning, however, appears to be in the further investigation of thyroid nodules which have been classified as cold or non-functioning by scanning with ^{99m}Tc or ^{131}I . The finding of avid ^{131}Cs uptake in such a nodule should heighten the suspicion of malignancy and, depending on the clinical circumstances, favour a decision that thyroidectomy be performed. Further, this finding should probably forewarn the surgeon about the desirability of a frozen section and the possibility of a more radical operation. Absence of ^{131}Cs uptake, on the other hand, though suggesting that malignancy is less likely, cannot be held to exclude it completely and should not be allowed to influence unduly the clinical evaluation of a thyroid swelling. If ^{131}Cs scanning of the thyroid is regarded in this way, the procedure would appear to offer a useful additional investigation which is worthy of continuing evaluation.

Case Report

A 49-year-old housewife was referred with a five-month history of increasing pain in the thoracic spine. She had no other complaints and was unaware of any thyroid swelling. On examination she was euthyroid. There was kyphosis of the thoracic spine, and a diffuse firm swelling was present on the right anterior chest wall. Two stony-hard nodules were palpated in the lower pole of the left lobe of the thyroid. The right lobe was palpable but softer in consistency. The thyroid gland was freely mobile and there were no palpable lymph nodes in the neck.

Radiological examination showed destruction of the fifth thoracic vertebra by an osteolytic lesion, and a similar lesion was present in the area of the right sacroiliac joint. The palpable mass on the anterior chest wall was seen to be an expanding tumour arising within the third rib.

A radiopertechnetate scan of the neck showed uniform isotope accumulation within the right lobe of the thyroid and the upper pole of the left. No uptake was seen in the palpable nodules. This pattern is illustrated in Fig. 2 A, in which the ^{99m}Tc accumulation is superimposed on a diagram of the thyroid as it appeared after total thyroidectomy. The radiocaesium scan (Fig. 3) showed an entirely different distribution from that of ^{99m}Tc , there being a localized area of uptake in the left lobe. This, however, did not correspond exactly with the palpable nodules which had failed to accumulate ^{99m}Tc (Fig. 2 B).

An open biopsy of the anterior chest lesion was performed and showed a well-differentiated thyroid follicular carcinoma. Subsequently, total thyroidectomy was performed. At operation a large nodule was found lying behind the left lobe, in addition to the nodules palpated previously. These are illustrated in Fig. 2 C, in which this "hidden" nodule corresponds to the area of avid ^{131}Cs accumulation previously observed. Histological examination confirmed that this hidden nodule was a follicular thyroid adenocarcinoma.

Before the thyroidectomy the patient had been given 500 μCi of ^{131}Cs . Portions of tissues were removed from different areas of the thyroid, including each of the nodules, as indicated in Fig. 2 C, and from three areas of the follicular carcinoma. The ^{131}Cs content of each specimen was determined and expressed as counts/sec./g. tissue (Table II). The ^{131}Cs content of the three benign nodules which had been palpable *in vivo* was much lower

TABLE II.—Radiocaesium Concentration in Different Areas of the Thyroid Gland

Specimen	Tissue	^{131}Cs Concentration (counts/sec./g.)
1	Normal thyroid	750
2	"	582
3	Calcified nodule	170
4	Benign adenoma	612
5	"	222
6	Follicular carcinoma	856
7	"	1,178
8	"	1,102
9	Lymph node containing follicular carcinoma	2,454

FIG. 2.—A, Representation of the distribution of ^{99m}Tc observed in a scan, superimposed on a diagram of the appearance of the thyroid as observed at total thyroidectomy. B, Representation of the distribution of ^{131}Cs superimposed on the same diagram. C, Diagram of the thyroid indicating sites of specimens removed for *in-vitro* ^{131}Cs counting. The site of the "hidden" carcinoma is indicated by the broken line.

FIG. 3.—Radiocaesium scan of the thyroid in patient presented in case report.

(a)

than that of the pieces of normal thyroid tissue. The ^{131}Cs accumulation in all the three portions of the follicular carcinoma, however, was significantly greater than that of the normal tissue. The highest ^{131}Cs concentration was found in a small lymph node adherent to the thyroid. Histological examination of this node showed that all lymph nodular tissue had been replaced by follicular carcinoma.

During convalescence scans of the skeleton were carried out two hours after the administration of mCi of $^{87\text{m}}\text{Sr}$. These showed increased isotope accumulation associated with the osteolytic lesions visualized radiographically. Subsequently, similar scans were obtained 72 hours after the administration of 5 mCi of ^{131}I . Localized ^{131}I uptake was found in these, corresponding exactly to the radiological lesions and to the areas of increased $^{87\text{m}}\text{Sr}$ uptake. In particular, localized ^{131}I uptake was observed in the anterior chest wall lesion (Fig. 4 A and B). No ^{131}I accumulation was detected in the neck. Before the administration of ^{131}I a further ^{131}Cs scan had been performed. As shown in Fig. 4 C, ^{131}Cs was demonstrated in the tumour metastasis in the chest wall, corresponding to the ^{131}I scan.

After the demonstration of tumour uptake of radioiodine the patient was given 150 mCi of ^{131}I . There was, however, clinical evidence of increasing spinal cord compression, for which the patient required laminectomy and removal of a portion of the metastatic deposit at T5. Histological examination of this specimen also showed metastatic thyroid adenocarcinoma.

Discussion

Though Charkes *et al.* (1965) did report scan evidence of positive ^{131}Cs accumulation in tumours in 7 out of 14 patients and, indeed, also found, as in the case described above, that the concentration of ^{131}Cs was increased in the cancerous tissue, they did note that the satisfactory scans were obtained only in large superficial tumours and not in those more deeply seated. This may be attributed principally to the physical characteristics of this radionuclide, which decays by electron capture to stable ^{131}Xe with the emission of a 29.8 KeV x-ray. Thus, if this radionuclide is to have a specific application for tumour detection, the thyroid gland is likely to prove a rewarding target. This concept is supported by the findings of Uchiyama *et al.* (1969), who reported ^{131}Cs uptake in 16 out of 20 malignant thyroid tumours which had failed to accumulate ^{131}I .

(b)

(c)

FIG. 4.—A, Radiograph of chest showing osteolytic lesion arising in the right third rib. B, Anterior scan of chest performed 72 hours after the administration of 5 mCi ^{131}I . C, Similar scan performed two hours after the administration of 500 μCi ^{131}Cs .

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